DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

95151d

Food and Drug Administration
555 Winderley Pl., Ste. 200
Maitland, Fl 32751

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

WARNING LETTER

FLA-05-13

December 7, 2004

Ms. Verena Oquendo
Executive Director
Lex, Inc.
7155 NW 77th Terrace
Medley, Florida 33166

Dear Ms. Oquendo:

During an inspection of your manufacturing facility located in Medley, Florida on June 28 through July 8, 2004, FDA Investigator Jennifer M. Menendez, determined that you manufacture numerous human drug products (OTC and Rx), which are drugs as defined by section 201(g)(1) of the Federal Food, Drug, and Cosmetic Act (the Act).

The drug products that you manufacture are adulterated within the meaning of section 501(a)(2)(B) of the Act because the methods used in, or the facilities or controls used for, their manufacture do not conform to the current good manufacturing practice (CGMP) regulations for drugs specified in Title 21, Code of Federal Regulations (CFR), Part 211.

The inspection revealed that there is no assurance that your products meet applicable standards of identity, strength, quality and purity because you failed to comply with CGMPs as follows:

1. **[21 CFR § 211.22(a) and (d)] Failure to have a quality control unit that shall have the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging material, labeling and drug products, and failure to follow the written responsibilities and procedures applicable to the quality control unit.**

   For example, the firm does not perform the responsibilities required by a quality control unit. Failures were observed in the following areas: SOPs have not been approved by the quality control unit, and the review of any complaints involving the possible failure of a drug product to meet any of its specifications has not been performed per SOP.

2. **[21 CFR § 211.25(a)] Failure to assure that each person engaged in the manufacture, processing, packing, or holding of a drug product shall have education, training, and experience, or any combination thereof, to enable that person to perform the assigned functions.**

   For example, according to the Executive Director of the firm, the employees have never received any type of CGMP training.

3. **[21 CFR § 211.84(a) and (d)] Failure to withhold from use each lot of components, drug product, containers, and closures until the lot has been sampled, tested, examined, and released by the quality control unit.**

   For example, the firm has not conducted at least one specific identity test to verify the identity of the active drug ingredients used to manufacture drug products. Additionally, the firm has never established the reliability of the supplier's analyses through appropriate validation of the supplier's test results at appropriate intervals.

4. **[21 CFR § 211.165(a)] Failure to have, for each batch of drug product, appropriate laboratory determination of satisfactory conformance to final specifications for the drug product, prior to release.**

   For example, your firm failed to determine the identity and strength of active ingredients for several products.

5. **[21 CFR § 211.165(b)] Failure to have appropriate laboratory testing , as necessary, of each batch of drug product required to be free of objectionable microorganisms.**

   For example, your firm failed to conduct microbial analysis and/or preservative assays on finished drug products as a criteria for release.

6. **[21 CFR § 211.160(b)] Failure to have laboratory controls that include the establishment of scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, and drug products conform to appropriate standards of identity, strength, quality, and purity.**

   For example, the firm does not have a sampling and test procedures designed to assure that the water from the purification system conforms to appropriate standards.

7. **[21 CFR § 211.113(a)] Failure to establish and follow appropriate written procedures designed to prevent microbiological contamination of drug products not required to be sterile.**

For example, operating procedures (i.e. meaningful microbial action limits, corrective action plan when action limits are exceeded) for the water purification system have never been established.

8. **[21 CFR § 211.100(a)] Failure to have written procedures for production and process control designed to assure that the drug products have the identity, strength, quality, and purity they purport to possess.**

   For example, the firm has not validated changes to the manufacturing processes, including scale up of batches.

9. **[21 CFR § 211.166(a)] Failure to implement a testing program designed to assess the stability characteristics of drug products.**

   For example, there is no written testing program designed to assess the stability characteristics for several drug products.

10. **[21 CFR § 211.137(a)] Failure to bear an expiration date determined by appropriate stability testing described in 21 CFR 211.166.**

    For example, there is a lack of data to support the firm's two and three year expiration date(s) for their drug products.

11. **[21 CFR § 211.188(b) Failure to prepare batch production and control records for each batch of drug product produced that include complete information relating to the production and control of each batch. These records shall include documentation that each significant step in the manufacture, processing, packing, or holding of the batch was accomplished.**

    For example, a statement of the actual yield is not calculated and recorded in the batch production record. Additionally, the batch production record does not include in-process results (i.e. weight checks) for each batch of drug product produced.

12. **[21 CFR § 211.192] Failure to have all drug product production and control records reviewed and approved by the quality control unit to determine compliance with all established, approved written procedures before a batch is released or distributed.**

    For example, there is no documentation that the batch production records have been reviewed and approved by the quality control unit.

Based on the intended uses included on labels for your firm's products, these products are drugs as defined in section 201(g) of the Act. We find the following OTC drug products to be new drugs as defined in section 201(p) of the Act because they are not generally recognized as safe and effective for their labeled uses, as explained below, and are in violation of final regulations covering these products, where applicable and cited below. Therefore, under section 505(a) of the Act, they may not be introduced or delivered into interstate commerce without approved new drug applications and are also misbranded under the Act, as follows:

1. LEX SODIUM BICARBONATE is offered for use as an antacid to alleviate heartburn, sour stomach, and/or acid indigestion. Based on these claims, the product is a drug that is subject to final regulations covering OTC antacid products (21 CFR Part 331). LEX SODIUM BICARBONATE is misbranded under sections of the Act as follows:

   502(a) because it fails to bear the term "antacid" as the required statement of identity (21 CFR § 331.30(a));

   502(f)(1) because the labeled directions for use do not specify a maximum daily dosage in accordance with 21 CFR § 201.5(d) and as further described by 21 CFR § 331.11(k)(1);

   502(f)(2) because it fails to bear the required warning regarding maximum daily dose of the product and the length of time the daily dose may be used (21 CFR § 331.30(c)(1)); and

   502(c) because it is not labeled in the Drug Facts format as required by 21 CFR § 201.66.

2. LEX EUCALYPTUS OIL Aromatic NF is offered for external use as an "antiseptic especially for the treatment of infections of the upper respiratory tract and certain forms of skin disease." We are not aware of substantial scientific evidence that eucalyptus oil is generally recognized as safe and effective for the treatment of infections in the upper respiratory tract or of any skin diseases. The ingredient has not been covered under the OTC Drug Review for these claims.

3. PHENYDEX PHYSICIANS [sic] SAMPLE contains dextromethorphan hydrobromide, guaifenesin, phenylephrine hydrochloride and pyrilamine maleate, and is offered as an antitussive, expectorant, nasal decongestant, and antihistamine. PHENYDEX Pediatric contains dextromethorphan hydrobromide, guaifenesin, and phenylephrine hydrochloride, and is offered as an antitussive, expectorant and decongestant. PHENYDEX Pediatric Drops contains dextromethorphan hydrobromide, guaifenesin, and phenylephrine hydrochloride and is offered as an antitussive, expectorant and decongestant.

a. The labels for PHENYDEX PHYSICIANS [sic] SAMPLE, PHENYDEX Pediatric, and PHENYDEX Pediatric Drops each bear the statement "Rx Only." These products are subject to final regulations covering OTC antihistamine, antitussive, expectorant and nasal decongestant products found at 21 CFR Part 341. All of the active ingredients and claims for these products are covered under these regulations. These products are, therefore, not entitled to bear the "Rx only" legend because they can be marketed as OTC drugs. As such, they are misbranded under section 503(b)(4)(B).

b. PHENYDEX PHYSICIANS [sic] SAMPLE and PHENYDEX Pediatric are also misbranded under section 502(a) because they contain aspartame, but their labels do not specify the amount of phenylalanine per dosage unit (21 CFR § 201.21(b)). The products are also misbranded under section 502(a) because the indications "headings" for each fails to bear any reference to the antihistamine uses (21 CFR § 341.72(b)).

c. PHENYDEX PHYSICIANS [sic] SAMPLE is also misbranded under section 502(f)(1) because its labeling fails to bear complete adequate directions for use as required by regulations for use as an antihistamine (21 CFR § 341.72(d)(11)), antitussive (21 CFR § 341.74(d)(1)(iii)), expectorant (21 CFR § 341.78(d)), and nasal decongestant (21 CFR § 341.80(d)(1)).

d. PHENYDEX Pediatric is misbranded under section 502(f)(2) because it fails to bear any of the required warnings for antihistamines (21 CFR § 341.72(c)), antitussives [21 CFR §§ 341.74(c)], expectorants [21 CFR § 341.78(d)] , and nasal decongestants [21 CFR § 341.80(d)].

e. PHENYDEX Pediatric is misbranded under section 502(a) because the "indications" heading fails to bear any information regarding antitussives [21 CFR § 341.74(b)]. PHENYDEX Pediatric is further misbranded under section 502(f)(2) because the statement "Do not exceed recommended dosage" is not in boldface type as required [21 CFR § 341.80(c)(1)(ii)]; and because it either fails to bear the following required warnings, or fails to bear the complete warnings in the wording required by the regulations:

- Accidental ingestion warning – 21 CFR § 330.1(g);
- Antihistamine warnings – 21 CFR § 341.72(c).

f. PHENYDEX Pediatric Drops product is misbranded under section 502(f)(2) of the Act because it either fails to bear the following warnings or the specific required wording for the warnings:

- Expectorant warnings – 21 CFR § 341.78(c);
- Nasal decongestant warnings – 21 CFR § 341.80(c).

4. LEX BORIC ACID POWDER is offered for use as an antifungal agent. Based on this intended use, the product is a drug and subject to the final regulations covering OTC topical antifungal drug products found in 21 CFR, Subpart C. Boric acid is the sole ingredient. Boric acid is not permitted as an active ingredient in the final regulations, 21 CFR §333.210. Further, the product's labeling for the statement of identity, indications, warning, and directions does not comply with the final regulations (21 CFR § 333.250 (a) - (d)). The product is also misbranded under section 502(f)(1) and 502(f)(2) of the Act because it fails to bear adequate direction for use for the indication noted above and the required warning.

5. Based on the label claims on the LEX Agua De Alibour label, such as, "May be applied to the skin for the treatment of acne, dandruff, poison ivy, lupus erythematosus and impetigo," it is a drug and is subject to final regulations covering topical OTC acne drug products (21 CFR Part 333 Subpart B), the drug products for the Control of Dandruff, Seborrheic Dermatitis, Psoriasis (21 CFR Part 358 Subpart H) and the topical antifungal drug products (21 CFR Part 333, Subpart C). None of the listed ingredients is permitted as an active ingredient under the mentioned final regulations (21 CFR §§ 333.310, 358.710 (a), and 333.210). Further, the labeling for the statement of identity, indications, warnings, and directions does not comply with the final regulations (21 CFR §§ 333.350 (a) - (d), 358.750 (a) - (d), and 333.250 (a) - (d)). The product is also misbranded under section 502(f)(1) and 502(f)(2) because it fails to bear adequate direction of use for the indications noted above and the required warnings. The skin conditions of lupus erythematosus and impetigo are not covered by the above mentioned final regulations.

It is your responsibility as a drug manufacturer to assure that all requirements of the CGMP regulations are met. You are also responsible for ensuring that all of the drug products you manufacture are safe and effective for all of their labeled claims.

Other Federal agencies are routinely advised of Warning Letters issued so that they may take this information into account when considering the award of contracts. Additionally, pending applications for Agency approval (NDA, ANDA, SNDA, etc.) or export approval requests may not be approved.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to all requirements of the Act and regulations. You should take prompt action to correct these violations. Failure to correct these violations may result in regulatory action, including seizure and/or injunction, without further notice.

Please notify this office in writing within fifteen (15) working days of receipt of this letter, of the specific steps that you have taken to correct these violations and to prevent the recurrence of similar violations. If corrective action cannot be completed within fifteen working days, state the reason for the delay and the time within which corrections will be completed.

Your reply should be directed to Timothy J. Couzins, Compliance Officer, U.S. Food and Drug Administration, 555 Winderley Place, Suite 200, Maitland, Florida, 32751, telephone (407) 475-4728.

Sincerely,

Emma R. Singleton
Director, Florida District